ACRYLAMIDE
(Group 2A)

For definition of Groups, see Preamble Evaluation.

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CAS No.: 79-06-1
Chem. Abstr. Name: 2-Propenamide

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Acrylamide has been produced since the 1950s by hydration of acrylonitrile. It is used mainly to produce water-soluble polyacrylamides used as flocculents for clarifying drinking-water, for treating municipal and industrial waste waters and as flow control agents in oil-well operations. Other major uses of acrylamide are in soil stabilization, in grout for repairing sewers and in acrylamide gels used in biotechnology laboratories. The major routes of exposure at the workplace appear to be dermal absorption of acrylamide monomer from solution and inhalation of dry monomer or aerosols of acrylamide solution. Exposure occurs during acrylamide and polyacrylamide manufacture, during acrylamide grouting and during laboratory preparation of polyacrylamide gels.

5.2 Human carcinogenicity data

Two cohort mortality studies were conducted among workers exposed to acrylamide. The first showed no significant excess of cancer but suffered from small size, short duration of exposure and short latency. In the other study, in one Dutch and three US plants, a nonsignificant increase was seen in deaths from pancreatic cancer, but there was no trend with increasing exposure.

5.3 Animal carcinogenicity data

Acrylamide was tested for carcinogenicity in one experiment in rats by oral administration. It increased the incidences of peritoneal mesotheliomas found in the region of the testis and of follicular adenomas of the thyroid in males and of thyroid follicular tumours, mammary tumours, glial tumours of the central nervous system, oral cavity papillomas, uterine adenocarcinomas and clitoral gland adenomas in females. In screening bioassays, acrylamide, given either orally or intraperitoneally, increased both the incidence and multiplicity of lung tumours in strain A mice.

Acrylamide was also tested as an initiating agent for skin carcinogenesis after oral, intraperitoneal and topical administration to mice of one strain and after oral administration to mice of another strain, followed by topical treatment with 12-*O*-tetradecanoylphorbol 13-acetate. It induced a dose-related increase in the incidence of squamous-cell papillomas and carcinomas of the skin in all four experiments.

5.4 Other relevant data

In occupational settings, acrylamide is taken up both through the skin and by inhalation. Damage to

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both the central and peripheral nervous systems has been reported on several occasions in exposed humans and has been thoroughly studied in animals.

Acrylamide is metabolized *in vitro* and *in vivo* in mice, rats and humans to the epoxide, glycidamide. Both substances are equally distributed throughout the tissues and have half-lives of about 5 h in rats; acrylamide itself has also been shown to be uniformly distributed between tissues in several other species. The conversion of acrylamide to glycidamide is saturable, ranging from 50% at very low doses to 13% at 100 mg/kg bw in treated rats. Both agents are detoxified by glutathione conjugation, and glycidamide is also detoxified by hydrolysis. Both agents react directly with haemoglobin in vivo, but DNA adducts result only from the formation of glycidamide.

The presence of haemoglobin adducts of acrylamide was correlated with neurotoxicity in a group of highly exposed workers.

Acrylamide was not teratogenic to rats or mice after oral treatment of dams with doses up to the toxic level. It causes testicular atrophy, with damage to spermatids and mature spermatozoa. Reduced sperm motility, impaired fertility and dominant lethal mutations at the spermatozoa stage have also been reported in mice and rats. A single study in rats provides evidence that the testicular damage is not secondary to neurotoxicity, since testicular damage but not neurotoxicity was induced by injection of the reactive epoxide, glycidamide.

The genotoxicity of acrylamide has been studied extensively. It induces gene mutation, structural chromosomal aberrations, sister chromatid exchange and mitotic disturbances in mammalian cells *in vitro* in the presence or absence of exogenous metabolic systems. It induces structural chromosomal aberrations *in vivo* in both somatic and germ-line cells. Chromosomal aberrations and micronuclei were induced in mouse bone marrow and in premeiotic and postmeiotic cells. Treatment with acrylamide *in vivo* also caused somatic mutation in the spot test, heritable translocation and specific locus mutations in mice and dominant lethal mutations in both mice and rats in several studies. Acrylamide induces unscheduled DNA synthesis in rat spermatocytes *in vivo* but apparently not in rat hepatocytes; glycidamide induced unscheduled DNA synthesis in rat hepatocytes in one study *in vitro*. Acrylamide induces transformation in cultured mammalian cells. It does not induce mutation in bacteria, but glycidamide does in the absence of an exogenous metabolic system. Acrylamide induces sex-linked recessive lethal and somatic mutations in *Drosophila*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of acrylamide.

There is *sufficient evidence* in experimental animals for the carcinogenicity of acrylamide.

In making the overall evaluation, the Working Group took into consideration the following supporting evidence:

(i) Acrylamide and its metabolite glycidamide form covalent adducts with DNA in mice and rats.

(ii) Acrylamide and glycidamide form covalent adducts with haemoglobin in exposed humans and rats.

(iii) Acrylamide induces gene mutations and chromosomal aberrations in germ cells of mice and

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chromosomal aberrations in germ cells of rats and forms covalent adducts with protamines in germ cells of mice *in vivo*.

(iv) Acrylamide induces chromosomal aberrations in somatic cells of rodents *in vivo*.

(v) Acrylamide induces gene mutations and chromosomal aberrations in cultured cells *in vitro*.

(vi) Acrylamide induces cell transformation in mouse cell lines.

Overall evaluation

Acrylamide is *probably carcinogenic to humans (Group 2A)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluation: Suppl. 7 (1987) (p. 56)

Synonyms

- Acrylic acid amide
- Acrylic amide
- Ethylenecarboxamide
- Propenamide
- Propenoic acid amide
- Vinyl amide

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